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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/681,669	10/07/2003	Arthur J. Blume	2598-4000US4	7579

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EXAMINER	
TUNGATURTHI, PARITHOSH K	
ART UNIT	**PAPER NUMBER**
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/681,669	BLUME, ARTHUR J.	
	Examiner	Art Unit	
	Parithosh K. Tungaturthi	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *76-79* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *76-79* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The applicant has timely traversed the non-final rejection in the reply filed on 12/14/2006, and a response to the arguments is set forth.

2. Claims 1-75 have been cancelled

3. Claims 76-79 have been newly added and are under examination.

4. This office action consists of new grounds of rejections in view of newly added claims.

Priority

5. The applicants arguments in regard to priority on pages 6-7 are found persuasive. Hence the instant application is given the priority of 08/03/1994.

Rejections Withdrawn

6. The rejection of claims 47-50 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of amendments to the claims.

The claims have been cancelled.

7. The rejection of claims 47, 48 and 50 under 35 U.S.C. 102(b) as being anticipated by Shin and Morrison (Proc. Natl. Acad Sci USA. 1990. 87:5322-5326) is withdrawn in view of amendments to the claims.

The claims have been cancelled.

8. The rejection of claims 47-50 under 35 U.S.C. 103(a) as being unpatentable over Shin and Morrison (Proc. Natl. Acad Sci USA. 1990. 87:5322-5326) in view of George et al (Journal of Immunology. 1994, 152:1802) is withdrawn in view of amendments to the claims.

The claims have been cancelled.

Claim Objections

9. Claim 78 is objected to because of the following informalities: Two claims are numbered "78". Appropriate correction is required..

New Grounds of Rejections

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 76 and 78 are rejected under 35 U.S.C. 102(b) as being anticipated by Shin and Morrison (Proc. Natl. Acad Sci USA. 1990. 87:5322-5326).

The instant claims are interpreted to be drawn to rVab-Pep, wherein rVab comprises a Vl, Cl, Vh and a Ch, Pep is a peptide component; wherein said rVab

component binds to a first determinant of said target and said peptide component binds to a second determinant of said target; and further wherein the peptide component is bound to the carboxy terminus of the CI.

Shin and Morrison teach the expression and characterization of an antibody binding specificity joined to insulin-like growth factor 1 and the potential applications of such chimeric molecules for cellular targeting (title, in particular). Shin and Morrison teach chimeric molecules comprising IgG3-IGF1, wherein IGF1 is an insulin-like growth factor and IgG3 is the chimeric mouse-human anti-dansyl (anti-Dns) antibody (abstract, in particular), which inherently comprises a VI, CI, Vh and a Ch. Shin and Morrison teach that the simultaneous binding by the antibody combining site to the antigen on the surface of the tumor cell and by the hormone to the hormone receptor will increase the specificity of targeting (page 5325 column 2, in particular). Shin and Morrison teach IgG3-IGF1 chimeric protein that retain their specificity for the antigen Dns and the IGF1 receptor on the same target cell. Further Shin and Morrison teach that the IGF1 molecule can be conjugated to the C-terminus of the of the CL region (please see figure 2C, page 5324 in particular).

Thus, since the claims are drawn to a rVab-Pep molecule, wherein rVab comprises a VI, CI, Vh and a Ch, wherein the peptide component is bound to the carboxy terminus of the CI, Shin and Morrison anticipate the instant claims.

Response to Arguments:

The applicants argue that the Shin and Morrison antibody does not bind a target as does the rVab-Peps of the invention.....the IGF1 chimeric antibody is the whole molecule that endogenously binds the IGF1 receptor. There are additional sequences present that are not directly responsible for binding to a determinant of the receptor....the components of the Shin and Morrison antibody do not each bind a determinant to effect biological activity as does the rVab-Peps of the invention....each component of the rVab-Peps of the invention binds to the target and the binding of each is required to elicit the biological activity. (pages 10-11 of the response filed on 12/14/2006).

The above arguments are carefully considered but are not found persuasive. The claim recites a rVab-Pep, wherein rVab component comprises a VL, CL, Vh and CH1, and Pep is a peptide component. The recitation "for use in identifying a small organic molecule, which binds to a determinant of a pharmacological target" within the claim is considered as intended use; and as per MPEP 2105

> "a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 370 F.2d 576, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 312 F.2d 937, 939, 136 USPQ 458, 459 (CCPA 1963)"

Hence, the recitation "for use in .....target" is not given patentable weight and as such the claims are interpreted merely as a product claims drawn to rVab-Pep compound. Thus, Shin and Morrison comprise all the components as required by the claimed invention i.e. an antibody peptide conjugate wherein the antibody comprises a

Vl, Vl, Vh and Ch1 and a peptide conjugated to such antibody at the C-terminus, wherein the antibody-peptide conjugate bind to the antigen Dns and the IGF1 receptor on the same target cell.

Further, the arguments presented by the applicant in regard to the differences in the functional aspects of the claimed invention and the teachings of Shin and Morrison; the examiner would like to point out the purpose of such recitation within the claims and the arguments is irrelevant because the core of the invention, as the claims are written, is drawn to the rVab-Pep product which is clearly taught in Shin and Morrison.

12. Claims 76-78 are rejected under 35 U.S.C. 102(b) as being anticipated by Huston and Operman (WO 88/09344, Published 12/1/1988).

Claims 76 and 78 have been described supra. Claims 77 is drawn to an rVab conjugated to any peptide molecule wherein both the antibody and the peptide bind to the same target, wherein the peptide molecule is conjugated to the amino terminus of VH region.

Huston and Operman teach a method of linking bioactive proteins to antibodies wherein either the amino or carboxyl terminal ends of the antibody are attached to the bioactive amino acid sequence to provide a multifunctional protein (p. 18, p. 27; Fig. 2B), wherein the antibody can be single chain Fv fragments complete heavy or light chains or portions thereof (abstract; p. 18; p. 47). Huston and Operman also teach that the fusion protein is designed at the DNA level wherein the DNA sequences of the antibody and bioactive protein are fused using conventional techniques well known in

the art and can be expressed in appropriate prokaryotic hosts such as various strains of *E. coli* (p. 30, 32, and 46). The fusion protein comprises a linker between the V_L and V_H antibody domains and a linker between the antibody fragment and bioactive protein (p. 22, 24, 25, 27, 30, and Fig. 8). Further, Huston and Operman teach that the either the amino or carboxyl terminal end of the antibody is attached to an amino acid sequence that is bioactive or has some other function in order to produce a bifunctional protein (p. 18 bridging to p. 19). In addition, Huston and Operman teach that the bioactive amino acid peptide may consist of a binding protein in addition to many other components (pages 27-28, bridging paragraph).

Thus, since the claims are drawn to a rVab-Pep molecule, wherein rVab comprises a Vl, Cl, Vh and a Ch, wherein the peptide component is bound to either the carboxy or amino terminus or both, and because Huston and Operman teach a method of linking bioactive proteins to antibodies wherein either the amino or carboxyl terminal ends of the antibody are attached to the bioactive amino acid sequence to provide a multifunctional protein, wherein the bioactive amino acid peptide may consist of a binding protein.

Hence, Huston and Operman anticipate the instant claims.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. Claims 76-79 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Shin and Morrison (Proc. Natl. Acad Sci USA. 1990. 87:5322-5326) in view of Huston and Operman (WO 88/09344, Published 12/1/1988).

Claims 76-78 have been described supra. Claims 79 is drawn to an rVab conjugated to any peptide molecule wherein both the antibody and the peptide bind to the same target, wherein the peptide component is bound to both of the amino terminus of the VH and the carboxy terminus of the CL.

Shin and Morrison has been described supra. Shin and Morrison does not teach the conjugation of the peptide molecule to the N-terminus of the VH region of antibody or wherein the peptide component is bound to both of the amino terminus of the VH and the carboxy terminus of the CL. These deficiencies are made up for by Huston and Operman.

Huston and Operman has been described supra.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to produced an antibody conjugated to a peptide molecule, wherein the antibody and the peptide molecule bind to the same target as taught by Shin and Morrison, and Huston and Operman.

One of ordinary skill in the art would have been motivated and would have reasonable expectation of success to have produced an antibody conjugated to a peptide molecule wherein both the antibody and the peptide bind to the same target, wherein the peptide molecule is conjugated to the carboxy terminus of the CL region as taught by Shin and Morrison, because Shin and Morrison teach chimeric molecules comprising IgG3-IGF1, wherein IGF1 is an insulin-like growth factor that binds to IGF1 receptor and IgG3 is the chimeric mouse-human anti-dansyl (anti-Dns) antibody, wherein the IgG3 antibody comprises a Vl, Vl, Vh and Ch1.

In addition, one of ordinary skill in the art would have known to combine the teachings of Shin and Morrison and Huston and Operman because Shin and Morrison et al teach the conjugation of an insulin-like growth factor (a 7 kDa molecule) to the C-terminus of CL domain of IgG3 and Huston and Operman teach a method of linking bioactive proteins to antibodies wherein either the amino or carboxyl terminal ends of the antibody are attached to the bioactive amino acid sequence to provide a multifunctional protein.

Further, one of ordinary skill in the art would have been motivated and would have had a reasonable expectation of success to have combined the teachings of the above references because Shin and Morrison teach the conjugation of the peptide molecule to the C-terminus of the antibody and because Huston and Operman teach that the either the amino or carboxyl terminal end of the antibody is attached to an amino acid sequence that is bioactive or has some other function in order to produce a bifunctional protein.

Thus, because Huston and Operman teach that the binding effect of antibody does not alter when the amino acid peptide is linker either to the amino or carboxy terminus, it would have been obvious to one of ordinary skill in the art to conjugate the peptide at the C-terminus or N-terminus or at both ends.

Therefore, the invention as a whole, as interpreted, was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

16. No claims are allowed.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Parithosh K. Tungaturthi whose telephone number is 571-272-8789. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

19. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
Parithosh K. Tungaturthi Ph.D.
(571) 272-8789

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER